THE BRITISH JOURNAL
OF
DERMATOLOGY
MAY 1957

TREATMENT OF LUPUS ERYTHEMATOSUS WITH CHLOROQUINE.

Therapeutic Results and a Comparison of the Value of Chloroquine and Mepacrine.

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In a previous paper (Christiansen and Nielsen, 1956), we reported our results obtained in the treatment of lupus erythematosus (L.E.) with mepacrine (atabrine). We found that the effect of this drug was fully comparable with that obtained by treatment with other drugs reported in the literature, such as gold and bismuth, but that the frequency and types of side effects, particularly dermatitis, rendered mepacrine unsuitable as a therapeutic agent in L.E. In addition, a cosmetically unpleasant yellow pigmentation of the skin invariably accompanies treatment. It was therefore reasonable to select chloroquine, which is chemically related to mepacrine, for a clinical trial in order to see whether it was possible to retain the advantages of oral administration and at the same time to avoid the side effects and discomforts produced by mepacrine.

Numerous reports on the chloroquine treatment of L.E. are available (Table I), suggesting that chloroquine actually offers these advantages, and that its side effects are less troublesome than those produced by mepacrine. The present paper was written in an attempt to clarify this problem, and to make a direct comparison between mepacrine and chloroquine. In this comparison the following points will especially be considered :

(*a*) The immediate therapeutic results obtained in the two series at the conclusion of the first course of treatment with mepacrine and chloroquine.

(b) The types and frequency of side effects produced by the two drugs.

(*c*) The frequency and time of occurrence of relapse.

TABLE I.—*Lupus Erythematosus Treated with Chloroquine.*

	Number of cases.	Excellent. (A). No.	Excellent. (A). %	Improved. (B). No.	Improved. (B). %	No, or questionable effect. (C). No.	No, or questionable effect. (C). %	Positive results. (A + B). %
Goldman, Cole and Preston, 1953	12	7	58	—	—	5	42	58
Grupper, 1953	41	24	59	12	29	5	12	88
Harvey and Cochrane, 1954	30	18	60	4	13	8	27	73
Pillsbury and Jacobson, 1954	16	6	38	9	56	1	6	94
Rogers and Finn, 1954	45	30	67	9	20	6	13	87
Prakken and Molhuysen van der Walle, 1954	25	17	68	6	24	2	8	92
Bertlich, 1954	23	13	56	7	30	3	13	87
Thies, 1955	56	39	70	10	18	7	12	88
Lepper and Allende, 1956	29	22	76	2	7	5	17	83
Total	277	176	63	59	21	42	15	84
Present series	137	89	65	33	24	15	11	89

CASE MATERIAL.

The present therapeutic experiments were performed in close relation to the previously published experiments with mepacrine in the treatment of L.E.

From 1 July 1954 to 1 January 1956 all patients with fresh L.E. and those with relapsing or resistant L.E. previously given mepacrine were treated with chloroquine. In one case chloroquine had to be withdrawn because of dyspeptic symptoms after 5 days, but in the remainder the treatment was continued for a sufficient time to permit evaluation of the drug. In only six cases was the treatment interrupted within the first month for reasons such as intercurrent disease, or because the patients moved to another part of the country.

As the purpose of the present paper is to compare the results obtained with chloroquine and mepacrine, a close analysis of the two series of patients is necessary. Here we are facing the difficulty that a considerable number of the patients of the chloroquine series are also included in the mepacrine series. This group must be accepted as less amenable to therapy because it consists of patients who did not respond satisfactorily to mepacrine or who had relapsed. On the other hand, there are grounds for believing that the series of patients who were exclusively treated with chloroquine represents cases which were likely to give a good response to therapy.

The case material thus comprises the following three groups :

Group I.—Patients treated with mepacrine alone.

Group II.—Patients treated with chloroquine after preceding mepacrine therapy.

Group III.—Patients treated with chloroquine alone. An analysis of these groups is illustrated in Figs. 1 and 2.

Age.—In each of the three treatment groups, the youngest patient was 19, 20 and 4 years, respectively, and the oldest patient 77, 77 and 79 years, respectively. The only difference between the three groups was that in Group III there were two children, aged 4 and 10 years. The ages of the majority of the patients in all three groups ranged from 35 to 50 years (Fig. 1).

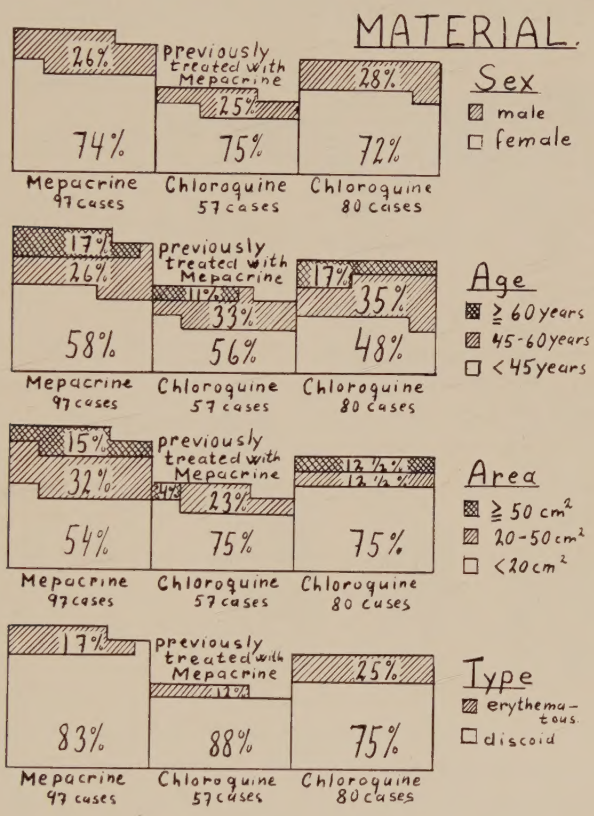


Fig. 1.

Type.—There were no subacute cases. The relatively few erythematous cases in Group II is in agreement with the fact that this form is more amenable to treatment and therefore had, to some extent, been eliminated by the preceding mepacrine therapy (Fig. 1).

Duration.—The duration of the disease prior to institution of therapy was obviously somewhat longer in Group II, since the patients in this group had been under treatment and observation for 12 months or more prior to chloroquine therapy. Apart from this, the duration of the disease seemed to be fairly uniform in the three groups (Fig. 2).

The distribution of sex and area involved is shown in Fig. 1, and of location in Fig. 2.

Thus, the three groups seemed to be of fairly uniform composition, apart from the fact that Group II may to a certain extent be regarded as less, and Group III as more, amenable to treatment than Group I. If Groups II and III are considered jointly, the two opposed tendencies will roughly neutralize each other, and a comparison between Group I on the one hand and Groups II and III on the other will thus be possible.

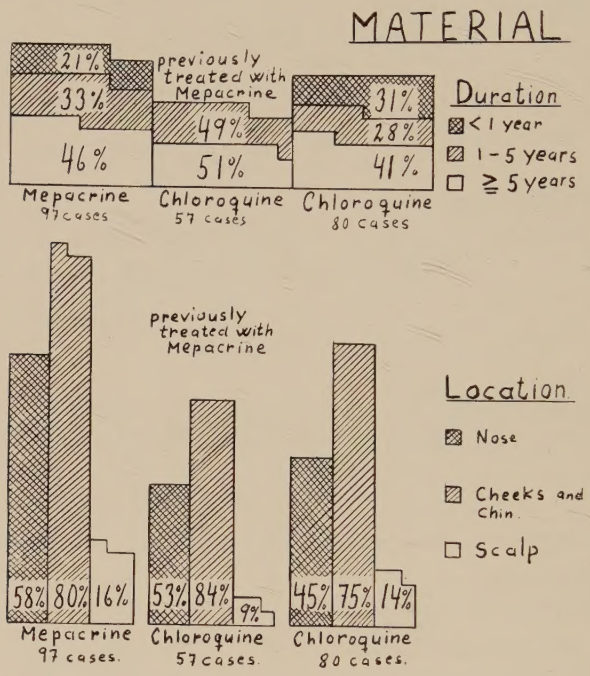


FIG. 2.

TREATMENT.

The treatment was not carried out according to any rigid formula because of variations in body weight and tolerance. We began with a daily test dose, which in adults was usually 250 mg. of chloroquine diphosphate, equal to 150 mg. of chloroquine base. If this daily dose was tolerated without discomfort for a few days, the dose was increased to 500 mg. of chloroquine diphosphate in men and large women and to 750 mg. in very large men. This daily dose was continued throughout unless side effects made a reduction necessary.

Treatment was stopped either when the patient became symptom-free, or when the condition in spite of prolonged treatment became stationary. Only in a few cases had the drug to be withdrawn because of side effects (see below). In seven patients the treatment was not finished at the time of the present analysis, but as they otherwise fall within the scope of the trial, they were

included to avoid the introduction of any bias by their exclusion. These patients must obviously be excluded in the consideration of relapse.

When the size of the daily dose had been determined the treatment was continued at home and the patients returned for observation once a month. The average duration of treatment was somewhat longer in the patients who were treated with chloroquine than in those treated exclusively with mepacrine (Table II).

TABLE II.

		Chloroquine treatment.	
	Mepacrine treatment.	Previous treatment with mepacrine.	No previous treatment with mepacrine.
Average duration of treatment, in weeks .	18	29	23
Average total dose, in g. . . .	18	53	49

RESULTS OF TREATMENT.

In the analysis of results we used the same method as in the study on mepacrine treatment of L.E. (Christiansen and Nielsen, 1956), the effect of treatment being assessed in each patient on the basis of erythema, infiltration, circumscription, scaling, and follicular keratosis.

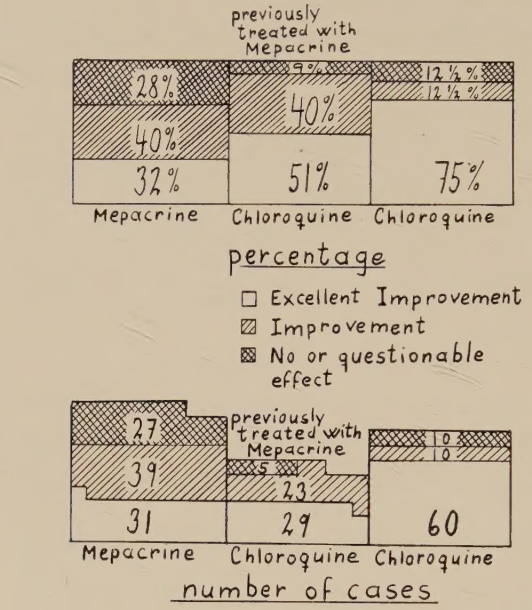
These results are shown in Fig. 3, which shows both relative and absolute values.

On a direct comparison of the results in Group I with those in Groups II and III, chloroquine seems to be far superior to mepacrine. If χ^2 is calculated for Group I compared with Groups II and III, respectively, the first calculation gives $\chi^2 = 9{\cdot}8$ ($p < 0{\cdot}01$) and the second $\chi^2 = 31{\cdot}9$ ($p < 0{\cdot}001$), i.e., the chances are less than 1 in 100 that the difference between Groups I and II is due to coincidence, and less than 1 in 1000 that the difference between Groups I and III is due to coincidence. As either of the two groups treated with chloroquine is better than the group treated exclusively with mepacrine, the sum of these two groups must also be definitely better than Group I.

Of the 89 patients who in Groups II and III obtained excellent improvement, not less than 57 (42%) were symptom-free at the conclusion of the treatment. For comparison, in the mepacrine-treated Group I only 11 out of 97 patients (11%) had obtained freedom of symptoms at the end of the first course of treatment. In Group III 39 patients (49%) were completely symptom-free at the end of the first course of treatment. Thus, the better results of chloroquine treatment cannot be ascribed to the fact that it was given as a supplement to mepacrine treatment, as in Group II.

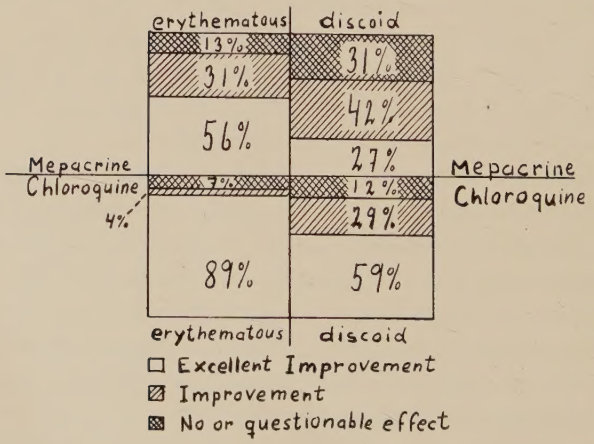
As in the series treated with mepacrine, we subjected the results of therapy obtained in the chloroquine series to a closer analysis in respect of sex, age, type and duration of disease, and the extent and localization of the lesion. The only one of these factors which seemed to influence the therapeutic result was

the type (Fig. 4). In the mepacrine-treated group we thought that the oldest age group responded considerably better than the younger—especially the youngest group. A similar observation was not made in the chloroquine series.



Results of Treatment

FIG. 3.



Results of Treatment in Relation to Type

FIG. 4.

Since the type of the lesion influences the therapeutic result, it is worth emphasizing that the two series showed good agreement with regard to this factor. The analysis as to sex, age, duration, extent and localization did not give any positive information.

Side Effects.

In mepacrine treatment we found that yellowing of the skin was a harmless but inevitable sequel. This is completely avoided in the chloroquine treatment, a thing which is greatly appreciated by the patients who have tried both drugs.

Table III shows a survey of the most important side effects observed in the patients.

Table III.—*Side Effects of Mepacrine and Chloroquine in the Treatment of Lupus Erythematosus.*

	Mepacrine (97 cases).			Chloroquine. Previous treatment with mepacrine (57 cases).			Chloroquine. No previous treatment with mepacrine (80 cases).		
	Patients		Withdrawal of drug.	Patients		Withdrawal of drug.	Patients		Withdrawal of drug.
	No.	%		No.	%		No.	%	
Flickering before the eyes, difficulty in visual accommodation, dizziness	—	—	—	8	14	0	15	19	0
Dyspepsia	16	17	7	14	25	2	21	26	0
Dermatitis	5	5	5	—	—	—	—	—	—
Disorders of sweating	8	8	0	—	—	—	—	—	—
Nervous disturbances	—	—	—	1	0·5	0	4	5	0
Itching of the skin	—	—	—	—	—	—	4	5	0

Severe generalised dermatitis occurred in 5% of the patients in the mepacrine series, but was not observed in any of the patients in the chloroquine series. Nor was chloroquine treatment followed by any disorder of sweating, which was observed in 8% in the mepacrine series. Dyspepsia was slightly more common after chloroquine than after mepacrine treatment, but the symptoms were less severe ; in most cases it was possible to continue treatment by a reduction of the dose or after a brief interruption.

After having been treated for some time with chloroquine, some patients complained of flickering before the eyes, dizziness, difficulty in visual accommodation, and other eye symptoms. This was not observed in the mepacrine series, and disappeared after reduction or fractionation of the dose or after a brief interruption ; permanent withdrawal of the drug was never necessary and presumably the symptoms are due to " supersaturation " with chloroquine. A few patients treated with chloroquine complained of nervous or emotional disturbances, such as restlessness, insomnia, nightmares, tremor of the hands,

and headache. Transitory itching of the skin developed in a few patients. Bleaching of the scalp hair, eyebrows and eyelashes occurred in three blond patients during the chloroquine treatment. After the termination of the treatment the hairs resumed their normal colour.

In recapitulation, the side effects of chloroquine treatment were less serious than those with mepacrine, but they were, perhaps, slightly more common. When the following measures were taken, the side effects of chloroquine could in most cases be reduced to a minimum which made it possible to complete the course of treatment :

(*a*) The chloroquine tablets should not be taken on an empty stomach.

(*b*) The daily doses may be given fractionated, for example $\frac{1}{2}$ or $\frac{1}{4}$ tablet at a time.

(*c*) The administration of chloroquine may be interrupted for a short period.

Problems Related to Dosage.

In the mepacrine series we found that the treatment should be continued until a total dose of about 25 g. had been given, corresponding to duration of treatment of about 25 weeks.

Chloroquine produced freedom of symptoms more often than mepacrine. When this has been attained, it is easy to decide when the treatment can be terminated if only the therapeutic result is to be considered. The problem is much more difficult if the risk of relapse is also to be taken into account. Another difficult problem is to decide how long treatment should be continued if the patient does not become symptom-free.

Table IV.—*Distribution of the Patients according to Total Dose and Therapeutic Result.*

Total dose, in g.	Under 50.	50–100.	100–150.	Over 150.
Number of patients	97	20	12	8
Excellent improvement	67 (+134 p.)	12 (+24 p.)	8 (+16 p.)	2 (+4 p.)
Improvement	24 (+24 p.)	5 (+5 p.)	2 (+2 p.)	2 (+2 p.)
No, or questionable improvement	6 (−12 p.)	3 (−6 p.)	2 (−4 p.)	4 (−8 p.)
Sum of points*	+146	+23	+14	−2

* The sum of points was obtained by giving +2 points to each case showing excellent improvement, +1 point to each case showing improvement, and −2 points to each case showing no definite signs of improvement.

An attempt was made to solve these problems by the evaluation shown in Table IV, in which we applied the method used in the mepacrine series. Up to 100–150 g. of chloroquine diphosphate it seems as if the higher dosage increased the number of favourable results. This corresponds to a duration of treatment ranging from 7 to 11 months, considerably longer than the 4 months which we found in the same way for mepacrine treatment.

Relapses.

The analysis of the mepacrine series revealed 80% of relapses in a 12-month observation period, chiefly during the first few months after the conclusion of treatment. The relapses did not show any seasonal variation. The average length of the observation period was 9·7 months.

In the chloroquine series the average length of the observation period from the conclusion of treatment was 8·6 months. It appears from Table V that in

Table V.—*Survey of Relapses.*

Time of Occurrence of Relapse in Relation to Time of Year.

	Month.											
	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Number of relapses	7	5	8	11	12	5	8	1	4	6	2	3

Time of Occurrence of Relapse in Relation to Termination of Therapy.

	Number of months after termination of therapy.																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Number of relapses	16	9	11	7	5	6	4	7	3	0	1	1	0	0	0	1	1	0

this series, too, the relapses occurred principally during the first few months. One should note, however, that the periods of observation were not of the same length in all the patients, so that all early relapses are recorded here, whereas later relapses were revealed only among patients with a longer period of observation. Of the patients who were observed for more than 12 months, the majority of the relapses occurred within the first 6 months. Relapses occurred more often in the spring months of April and May.

The frequency of relapse after an observation period of 12 months is shown in Table VI.

Table VI.

Period of observation in months.	Mepacrine series.		Chloroquine series.	
	Cases.	Relapses.	Cases.	Relapses.
Under 6	13	6 (46%)	33	10 (30%)
6–12	34	27 (80%)	42	29 (69%)
Over 12	23	18 (78%)	40	33 (83%)

From this it seems that the frequency of relapse is roughly the same in the two series, viz. about 80% after an observation period of 12 months.

Maintenance Therapy.

We have previously expressed the view that it would be desirable to use small doses of chloroquine in long-term treatment of L.E. patients. This was possible only to a minor extent since the present study primarily aimed at a

direct comparison of the two drugs. If we had concluded the chloroquine course with a lower maintenance dose, the observation of the relapses could not have been made under equal conditions in the two series.

However, in cases where the patients returned for treatment of relapsing L.E. after chloroquine therapy, the second course was followed by a lower maintenance dose for at least 3 months. We changed over to maintenance therapy when the condition had remained stationary for some time, or when the patient had become symptom-free.

Two different maintenance doses were used ; all patients born on even dates were given 125 mg. ($\frac{1}{2}$ tablet) of chloroquine diphosphate daily, while those born on uneven dates were given 500 mg. (2 tablets) once weekly (Table VII).

TABLE VII.

Maintenance dose of chloroquine diphosphate.	125 mg. daily = 875 mg. weekly.	500 mg. once weekly.
Number of patients	17	13
Number of relapses—		
1st month	3	4
2nd „	0	2
3rd „	1	3
4th „	3	0
Total	7 (41%)	9 (70%)

Obviously, it is difficult to draw definite conclusions from the few patients who received maintenance therapy, but it seems clear that neither of the doses suppressed the tendency to relapse to any considerable extent. The difference between the two groups is not significant. In general, it seems that if a maintenance course is to be given, for example, during the spring, a dose similar to that used under actual therapy must be advised.

LABORATORY EXAMINATIONS.

As in the mepacrine series, several routine laboratory examinations were made in the patients treated with chloroquine. Determination of haemoglobin level and erythrocyte sedimentation and platelet, white-cell and differential counts were performed in all adult patients before, during and after treatment.

Most of the patients were also subjected to the following liver-function tests : thymol turbidity test, Takata-Ara's test, determination of alkaline phosphatase, cephalin-cholesterol flocculation test, and fractional serum protein determination.

As a case of methaemoglobinaemia following chloroquine therapy has been reported (Ayres and Ayres, 1955), we have recently studied our patients for this side reaction.

The results of the laboratory examinations were in close agreement with those observed in the mepacrine series. As we were unable to demonstrate any parallel between the laboratory findings and the therapeutic results or side effects, these findings are not reported here. Suffice it to mention that none of 55 patients studied for methaemoglobinaemia after prolonged chloroquine treatment revealed this side reaction.

Discussion and Conclusions.

In the analysis of the mepacrine series we concluded that that treatment gave results which were comparable with those previously reported for other drugs, such as gold chloride and bismuth ; but that the frequency and types of side effects in mepacrine therapy were so considerable that the drug could not be recommended for general use in the treatment of L.E.

We can now offer the patients another form of oral treatment which is not beset with untoward reactions to the same extent as mepacrine therapy. The most important differences between the two forms of therapy are considered below.

Therapeutic results.—The results of treatment with chloroquine are essentially better than those obtained with mepacrine.

Side effects.—Chloroquine treatment is not accompanied by the yellow pigmentation of the skin and does not seem to produce disturbances in the sweat secretion, which are frequently seen with mepacrine. Severe dermatitis, which occurred in 5% of the mepacrine-treated patients, did not occur after chloroquine treatment. A few cases of dermatitis following chloroquine therapy have been reported (Ayres and Ayres, 1955 ; Craige *et al.*, 1948), but these seem to be less severe than mepacrine dermatitis and to occur less often.

Dyspeptic symptoms may be slightly more frequent in chloroquine than in mepacrine therapy, but seem to be less severe.

Chloroquine treatment is relatively often accompanied by emotional or mild nervous disturbances. Although we did not observe such reactions in our mepacrine series, they have been reported to occur with that drug (Grupper, 1955).

On the whole, it may be said that the side effects of chloroquine are less troublesome and less serious than those produced by mepacrine. This may be because chloroquine is less prone to concentrate in parenchymatous organs (Berliner *et al.*, 1948). Thus, it is easier to keep the serum concentration at a therapeutic level, and if side effects do develop, chloroquine will be eliminated more rapidly than mepacrine.

Frequency of relapse.—Both drugs give a relatively high frequency of relapse ; in both series about 80% of relapses have been encountered after an observation period of 12 months.

Thus, in most respects chloroquine seems to be superior to mepacrine in the treatment of L.E. It must be presumed that the better results of treatment are to some extent due to the fact that chloroquine is less toxic than mepacrine, which makes it possible to give higher doses over a prolonged period.

Both drugs seem to have a pronounced symptomatic effect on L.E. and must therefore be considered to be our most efficacious therapeutic agents against localized L.E. at the present time. Owing to the fewer side effects and better therapeutic action chloroquine must be preferred to mepacrine. However, it seems necessary to be on the look-out for new and still better methods of treatment in L.E. since the tendency to relapse is very great with the two drugs considered here.

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LYMPHOCYTIC INFILTRATION OF THE SKIN (JESSNER).

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At a meeting of the Bronx Dermatological Society, Jessner and Kanof (1953) presented an account of a condition which they named Lymphocytic Infiltration of the Skin. Together with Sawicky they had studied a group of cases with similar features for about ten years. Jessner has not published a full account of his patients but he summarized the cases as follows. "The lesions are flat, discoid, more or less elevated, pinkish to reddish-brown, starting as papules, expanding peripherally, sometimes clearing in the center, sometimes showing a circinate arrangement. The surface is smooth, occasionally uneven. There is no follicular hyperkeratosis. The consistency is firm. There may be only one, a few, or numerous lesions. They persist for weeks or months or longer, disappear without sequelae, and may recur in the same or other areas and cause practically no subjective symptoms. The face is obviously the area of predeliction but other parts of the body may or may not be affected."

Two years previously, Garb (1951) showed a patient to the same society as Lymphoblastoma and in spite of some unusual features, Kanof said it was the same as Jessner's cases. Eight cases have since been demonstrated at American dermatological meetings where others said they had seen similar cases.

The first case to be reported in England was shown at the Royal Society of Medicine in 1955 (Calnan, 1956). The purpose of this paper is to report seven additional cases and to emphasize that the condition is by no means rare.

Case Reports.

Case 1 (Calnan, 1956).—An hotel manager aged 40.

History.—For four years he has had red lumpy lesions on the back. They sometimes clear entirely for short periods, but usually are present in various stages of evolution and resolution.

On examination.—Bright pinkish red raised infiltrated lesions, arranged as papules, plaques or rings are present on the back, with two lesions on left arm. No enlarged lymph glands, liver, or spleen found.

Investigations.—Blood count, sedimentation rate and proteins normal; no L.E. cells found; W.R. negative.

Histology (Dr. Haber).—The epidermis appears normal. The vascular network of the corium is enveloped in a thick mantle of round cells. The vessels themselves do not show any abnormality.

Case 2.—A policeman aged 37.

For three years he has had a pink papular eruption on the cheeks especially on the zygomatic area (Fig. 1) and on the forearms and back of the chest. Lesions have come and gone in about ten days. The lesions sometimes cleared up during treatment

Fig. 1.—Typical appearance of aggregated papules over the zygomatic area (Case 2).

with chloroquine, but at other times recurred while he was still taking the drug. The diagnosis of polymorphic light eruption was made at one time.

Histology.—Patches of lymphocytic infiltration in the dermis. Epidermis normal.

Case 3.—An accountant aged 33.

For three years he had had annular or arcuate papular lesions on the back and sometimes on the malar areas. They are pinkish-red in colour and appear and disappear spontaneously, irrespective of treatment with chloroquine or x-ray, sulphapyridine or arsenic. The original diagnosis was lymphocytic reticulosis or a chronic annular erythema.

Histology.—A lymphocytic infiltrate in the dermis.

Case 4.—An R.A.F. officer aged 40.

For six months he has had a circinate papular erythema over the right malar area. It appears and resolves at intervals of six weeks. There has been no response to 150 r x-ray.

Histology.—A patchy lymphocytic infiltrate.

Case 5.—A waiter aged 47.

For eighteen months there have been red papules on the cheeks, forehead and elbows. It has resolved and recurred.

Histology.—A marked lymphocytic infiltrate around blood vessels and appendages.

Case 6.—A commercial traveller aged 42.

For two and a half years he has had a papular eruption on the upper parts of the cheeks. He thought sunlight at the seaside made it worse on one occasion. It has not cleared up in winter but the patches have receded and recurred irrespective of season.

Histology.—A heavy lymphocytic infiltrate in the dermis. The epidermis is normal (Fig. 2.).

Fig. 2.—Dense lymphocytic infiltrate ; epidermis normal. × 27 (Case 6).

Case 7.—A clerk aged 47.

For four years he has had a recurrent eruption on the lumbar area, the left axilla, the right shoulder, and on one cheek, composed of pinkish papular rings, crescents or plaques which vary but have never completely cleared.

Case 8.—A man aged 35.

For eight years he has had a discoid and annular eruption over the upper parts of the cheeks. The lesions are papular and have a smooth pink surface with no epidermal change. They remit and recur and have usually been worse in summer.

Clinical Features.

There is a heavy preponderance of males ; in twenty-one cases there were only two women. The age varies from 27 to 68 years, but in most cases is under 45.

The usual sites are the malar region and the back of the chest but the forehead, neck, mastoid region, arms, legs, chest or abdomen may be affected.

The lesions are aggregated erythematous papules or plaques varying in size from 2 mm. to 2 cm. in diameter and may be arranged in crescents or rings. Their colour is a uniform rose-pink and there is no scaling or other change.

The prognosis and course of the condition is variable. The patients give a history of some months up to about ten years (six months to eight years in our cases), with recurrences and remissions. Most cases show periods of freedom of a few weeks or months, but none have recovered permanently or for any considerable time.

Histology.

The epidermis is always normal. The entire network of vessels is enveloped in a dense mantle of lymphocytes ; this process may extend down to the fat and the tissue spaces of the dermis may also be permeated with lymphocytes.

Diagnosis.

From the clinical point of view, lupus erythematosus, a reticulosis, chronic annular erythemas, polymorphic light eruption, sarcoid and syphilis may have to be considered in the differential diagnosis. When the face is affected, cases are usually diagnosed as the papular type of lupus erythematosus or a light eruption ; when the lesions are on the body, as a reticulosis or an annular erythema. The most regular features which help to differentiate it are the uniform rose-red colour and the fact that the lesion consists entirely of erythematous papules which may be discrete or may be grouped into plaques, crescents or rings.

Histologically, however, sarcoid and syphilis can be excluded. Although the arrangement of the infiltrate is compatible with lupus erythematosus, the absence of epidermal changes makes one suspicious. It is impossible to exclude an early lymphocytic reticulosis or one of the annular erythemas, without clinical data.

The same appearances may be seen in insect-bite reactions. A patient has recently been described in Cuba (Quero and Blanco, 1955) with a lesion on the cheek which followed the bite of a " green fly " and which clinically and histologically conformed to Jessner's account.

Discussion.

Jessner deliberately coined the term lymphocytic infiltration of the skin as a non-committal name for these cases because nothing was known about their aetiology. They do not behave like lupus erythematosus, for there is never any epidermal change and atrophy does not develop even after many years. They do not regularly behave like an actinic eruption ; lesions appear on covered parts and are often unrelated to the sunny seasons. Mepacrine and chloroquine sometimes clear the eruption dramatically but do not consistently do so. Similarly, x-rays or any other therapy may seem effective in individual cases, but the case histories suggest that the condition runs a remittent course

irrespective of treatment over a number of years. No case has been reported to progress to lymphoblastoma or leukaemia. Kanof (personal communication) who studied his cases cannot add anything to Jessner's original views.

Bäfverstedt (1943) published a monograph entitled "Lymphadenosis Cutis Benigna," but I do not believe his cases have any relation to Jessner's either clinically or histologically.

The condition should be recognized as an entity because the patients can be given a benign prognosis, and may be assured that permanent changes in the skin will not occur. I felt content with these views until I recently saw a patient of Dr. Wigley's. She was a woman of 58 who first came to hospital in 1952. She had had an erythematous eruption on the trunk for six years and recently two bluish nodules had appeared. The pink lesions came and went spontaneously, and the nodules cleared with 200 r x-ray. The erythematous lesions have gone on recurring—a total duration of ten years now. They conform to lymphocytic infiltration of the skin, but she probably has a reticulosis. Only time will elucidate the problem.

I am indebted to Dr. G. B. Dowling, Dr. F. R. Bettley, Dr. H. J. Wallace, Dr. L. Forman, Dr. S. C. Gold, Dr. J. E. M. Wigley and Dr. E. W. Prossor Thomas for permission to include their cases in this survey. I am grateful to Dr. H. Haber for considerable help with the histology, and to Mr. R. J. Lunnon, photographer to the Institute of Dermatology for the photographs.

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THE TREATMENT OF LUPUS ERYTHEMATOSUS AND LYMPHOCYTIC INFILTRATION OF THE SKIN WITH A.P.A. 5533

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Since Prokoptchouk (1940) first introduced quinacrine hydrochloride (Atabrine, Mepacrine) in the treatment of lupus erythematosus, numerous publications have appeared attesting to the therapeutic efficacy of this drug. With the development of newer antimalarial agents, it was not long before additional reports indicated that chloroquine diphosphate (Aralen) was safer and as effective or more so in the management of this disease (Shee, 1953). In 1950, Surrey and Hammer synthesized and described hydroxychloroquine (Plaquenil), a 4-aminoquinoline similar to chloroquine diphosphate, but differing from the latter in that a hydroxyethyl group is substituted for one of the ethyl groups on the tertiary amino nitrogen.

During this past year, there have been several reports dealing with the therapeutic efficacy of Plaquenil (Mullins *et al.*, 1956 ; Cornbleet, 1956 ; Lewis and Frumess, 1956). In the present series, of 17 patients treated with Plaquenil, 14 had chronic discoid lupus erythematosus and 3 had lymphocytic infiltration of the skin (Jessner and Kanof, 1953). The clinical data and therapeutic results are recorded in Table I. Our results indicate that Plaquenil is as effective as mepacrine and chloroquine. Some patients responded better to one drug than to another and each produced some side effects. Since no drug is effective for all patients, it was hoped that there might be an increase in therapeutic efficacy and a decrease in untoward reactions if smaller amounts of all three antimalarials were combined. Such a combination might induce a synergistic therapeutic action. The purpose of this study was to evaluate the efficacy of A.P.A. 5533, a combination of mepacrine, Plaquenil and chloroquine in 10 patients with chronic discoid lupus erythematosus and 4 patients with lymphocytic infiltrations of the skin. Of these 14 white patients, 7 were men and 7 were women of ages ranging from 18 to 75 years. One tablet of A.P.A. 5533 contained one-fourth of the usual therapeutic dose of each antimalarial : mepacrine 25 mg., Plaquenil 50 mg. and chloroquine 65 mg. Although there was some slight variation in dosage, most patients were started on 2 tablets, four times daily, after meals and before retiring. As soon as there was definite evidence of clinical improvement. the daily dose was reduced by 2 tablets at two-week intervals until a minimum maintenance dose was determined. If marked side

TABLE I.—*Results of Treatment with Plaquenil, 400 mg. q.i.d.*

Case No.	Diagnosis.	Former therapy.	Plaquenil treatment.	
			Untoward reactions.	Improvement.
1	LE	None	Headache, nausea	Slight.
2	,,	Chloroquine	Headache	Poor.
3	,,	,,	None	Excellent.
4	,,	Mepacrine, chloroquine	Headache	,,
5	,,	Chloroquine	Diarrhoea	Good.
6	,,	None	None	Excellent.
7	LI	Mepacrine, chloroquine	Diarrhoea, nausea	,,
8	LE	Ditto	Nausea, diarrhoea	Slight.
9	LI	None	None	,,
10	LE	Chloroquine	Diarrhoea	Excellent.
11	,,	Mepacrine, chloroquine	,,	,,
12	LI	Chloroquine	,,	,,
13	LE	,,	None	Slight.
15	,,	Mepacrine, chloroquine	,,	Excellent.
16	,,	Chloroquine	Diarrhoea	Poor.
17	,,	Mepacrine, chloroquine	None	Excellent.
20	,,	Chloroquine	,,	,,

LE—Discoid lupus erythematosus.
LI—Lymphocytic infiltrations.

effects were noted, treatment was discontinued until all evidence of intolerance had subsided and then resumed at one-half the original dose. The clinical data and the therapeutic results are recorded in Table II.

Of the 10 patients with discoid lupus erythematosus, 7 obtained an excellent result with complete subsidence of all clinical activity. In 3 patients, there was no response to a daily dose of 8 tablets but an excellent improvement was noted when the dose was increased to 12 tablets daily. At the end of the first week, the dose was reduced to 8 tablets and the following week to a maintenance of 4 tablets daily. Two remained completely clear after several weeks of this maintenance dose while the third patient developed a recurrence with the decreased dosage ; this patient also had responded with only slight improvement to previous therapy with chloroquine and Plaquenil (Case 13). Of the 4 patients with lymphocytic infiltration of the skin, 3 showed complete clearing of the lesions but in one there was only slight improvement. The maximum clinical improvement was obtained within two weeks of therapy.

There were three cases of intolerable side effects. Two patients developed severe diarrhoea, vertigo and muscle pains on a dosage schedule of 8 tablets daily ; the third had no side effects at this dose but developed severe diarrhoea when it was increased to 12 tablets daily. In the remaining 11 patients, there were no complaints or there was only minimal discomfort consisting of mild diarrhoea, diplopia, nausea and some vertigo. In these instances, it was not

TABLE II.—*Comparative Results.*

Case No.	Diagnosis.	Chloroquine. Improvement.	Chloroquine. Side effects.	Plaquenil. Improvement.	Plaquenil. Side effects.	A.P.A. 5533. Dosage (tabs.).	A.P.A. 5533. Improvement.	A.P.A. 5533. Side effects.
2	LE	Good	Headache, Dysmenorrhea, vertigo	Poor	Headache	2 *q.i.d.*	Excellent	None.
3	,,	Slight	Vertigo, urticaria	Excellent	None	—	—	—
4	,,	Excellent	Diplopia	,,	Headache	2 *q.i.d.*	,,	Nausea.
5	,,	Poor	Nausea	Good	Nausea, diarrhoea	2 *q.i.d.*	,,	Diplopia.
7	LI	Excellent	,,	Excellent	Ditto	2 *q.i.d.*	Poor	Diarrhoea.
8	LE	Slight	,,	Slight	,,	2 *q.i.d.*	Good	Diplopia, diarrhoea.
10	,,	Excellent	None	Excellent	Diarrhoea	2 *q.i.d.*	Excellent	None.
11	,,	,,	Diarrhoea, diplopia	,,	,,	—	—	—
12	LI	,,	None	,,	,,	2 *q.i.d.*	Excellent	None.
13	LE	Poor	Urticaria	Poor	None	3 *q.i.d.*	Poor	,,
14	LI	Excellent	None	—	—	2 *q.i.d.*	Excellent	Diarrhoea, vertigo.
15	LE	,,	,,	Excellent	None	1 *q.i.d.*	,,	None.
16	,,	Good	,,	Poor	Diarrhoea	1 *q.i.d.*	,,	,,
17	,,	Excellent	Nausea, diplopia	Excellent	None	2 *q.i.d.*	,,	Vertigo, diplopia.
18	,,	,,	None	—	—	2 *q.i.d.*	Poor	Vertigo, muscle pain.
19	LI	—	—	—	—	3 *q.i.d.*	Excellent	Diplopia.
20	LE	Good	Nausea	Excellent	None	—	—	—

necessary to discontinue therapy. It is of special interest that six of these patients had developed marked side effects from previous antimalarial regimens administered according to our usual dosage :

	Daily dose (mg.)	Amount of drug in 8 tabs. of A.P.A. 5533. (mg.)
Mepacrine	300	200
Plaquenil	800–1600	400
Chloroquine	750	520

With the combined therapy contained in A.P.A. 5533 the recommended dose of Plaquenil was reduced by one-half or three-fourths, and the dose of mepacrine and chloroquine was reduced by approximately one-third.

In 16 patients it was possible to compare the therapeutic efficacy and the incidence of side reactions obtained with one or more of the three antimalarials when administered alone or in the triple combination. The combined tablet produced better results and was better tolerated than any of the three taken individually (Table II).

SUMMARY.

A.P.A. 5533, a mixture of mepacrine, Plaquenil and chloroquine, is effective in the treatment of chronic discoid lupus erythematosus and lymphocytic infiltration of the skin.

Although about three-fourths of the patients responded satisfactorily to mepacrine, chloroquine or Plaquenil alone, some did well with one but showed no improvement with another antimalarial.

Plaquenil appeared to be better tolerated than chloroquine, but the incidence of side effects was lowest with A.P.A. 5533 in spite of the high dosage schedules employed with the latter.

The incidence and severity of side reactions with A.P.A. 5533 depended on the daily dosage and the individual susceptibility of the patient.

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The A.P.A. 5533 (Atabrine-Plaquenil-Aralen) used in this study was furnished through the courtesy of the Department of Medical Research, Winthrop Laboratories, New York, N.Y.

THE AGE AND SEX INCIDENCE AND ANATOMICAL DISTRIBUTION OF ORAL LEUCOPLAKIA AND LICHEN PLANUS.

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Oral leucoplakia and lichen planus are usually diagnosed clinically and, although the clinical diagnosis is not always borne out by histological examination, it is convenient to classify most long-standing white lesions in the mouth under one or other of these headings. Owing to what may appear an inadequate basis for differentiation, the statistics which follow may be strongly criticized. However, considering that the same diagnostic methods apply throughout and that there is seldom any great doubt as to which category a particular lesion represents, it would be strange if the variations observed were entirely due to chance. The following account is an analysis of 148 consecutive cases observed in the Newcastle upon Tyne Dental Hospital. Eighty-one were diagnosed as leucoplakia and 67 as lichen planus.

The age and sex incidence of oral leucoplakia.

Of 60 male cases of leucoplakia, the youngest was 29 years of age and the oldest 83. Of 21 female cases the youngest was 31 and the oldest 81. The ages stated are those of the patients when first seen and it is probable that,

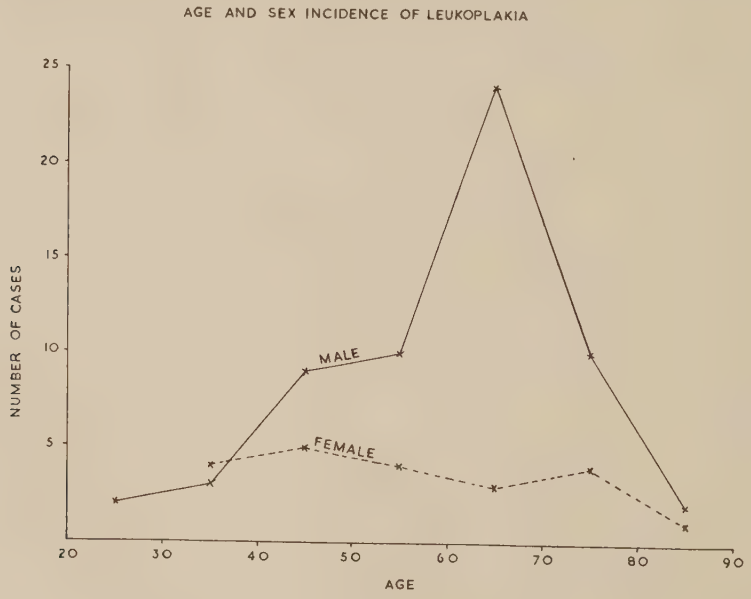

Fig. 1.

especially in the older patients, the lesions had been present for a considerable time before they were observed. In Fig. 1 the cases have been grouped in 10-year age periods and the pronounced variation in age incidence between the sexes is evident. The sharp ascent in the male curve to the 60–69 age group contrasts strongly with the apparent lack of influence of age in the women. It is interesting to speculate on what might be the eventual incidence if the normal life span were longer.

The anatomical distribution of oral leucoplakia.

The anatomical distribution of the lesions was recorded in 48 male patients and 19 female patients. The mouth was divided into seven zones and the findings are represented in Table I. It will be appreciated that patients commonly had lesions in more than one zone.

TABLE I.

		Total cases.	Lips.	Palate.	Cheek.	Tongue.	Alv-eolus.	Floor of mouth.	Fauces.
Male :	Number of cases	48	11	10	24	16	12	4	3
	% of cases		23	21	50	33	25	8	6
Female :	Number of cases	19	0	5	8	4	5	7	1
	% of cases		0	26	42	21	26	32	5

The only pronounced difference between male and female was in the lips, nearly a quarter of the male patients showing lesions in this area against none of the female patients, and in the floor of the mouth where a third of the female patients had lesions, an incidence four times as high as that in the male.

The age and sex incidence of oral lichen planus.

Of 21 male patients with oral lichen planus, the youngest was 21 years of age and the oldest 56. Of 44 female patients the youngest was 18 and the oldest 72. In Fig. 2 the cases have been divided into 10-year age groups as for leucoplakia ; the graph shows effectively the variation in sex incidence. The male cases show a peak in the 30 39 age period and an early falling off. The female cases rise to a peak in the 50–59 year group.

The anatomical distribution of oral lichen planus.

The situation of the oral lesions was studied in 15 of the male and 35 of the female cases. The same classification has been used in Table II as in that relating to leucoplakia.

TABLE II.

		Total.	Lips.	Palate.	Cheeks.	Tongue.	Mucosa.	Floor of mouth.	Fauces.
Male :	Number of cases	15	1	3	12	7	3	1	0
	% of cases	100	7	20	80	47	20	7	0
Female :	Number of cases	35	3	5	30	14	3	2	0
	% of cases	100	9	14	86	40	9	6	0

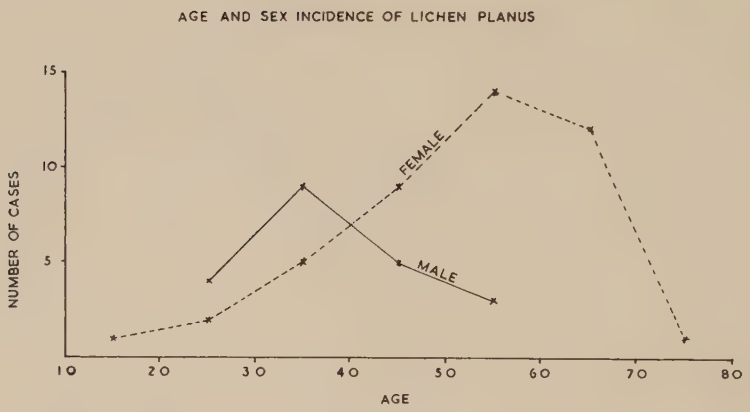

Fig. 2.

These figures indicate that the anatomical distribution is not greatly influenced by the sex of the patient but a tendency is observed in the female towards a somewhat more frequent occurrence on the cheeks and lips and a correspondingly reduced incidence elsewhere. The frequent occurrence of lesions on the cheeks and tongue is clearly demonstrated.

CONCLUSIONS.

The main conclusions to be drawn from this investigation may be summarized as follows :

Leucoplakia is three times as common in men as in women. The male cases reach a maximum in the 60–69 age group, 40% of the patients being first seen at that time. The incidence of leukoplakia in women does not appear to be influenced by age.

Lichen planus is twice as common in women as in men. The greatest number of male cases occur in the 30–39 age group. The greatest number of female cases occur in the 50–59 age group, at which age the condition is not common in men.

Leucoplakia of the lips is common in men but did not occur in any of the female cases in this study. Lesions in the floor of the mouth are present in one-third of female patients but in only one in twelve of male patients. Otherwise the distribution of leucoplakia and lichen planus is similar in both sexes.

Acknowledgement.

The author wishes to thank the Director of the Newcastle-upon-Tyne Dental Hospital for his permission to publish the material used in this article.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. Louis Forman.

17 May 1956.

Trichorrhexis Nodosa (Congenital and Inherited).—Dr. I. Martin-Scott.

T. L—, female, aged 7 years.

History.—Since birth her scalp hair has never grown to a normal length, and she has never needed to have it cut. She has not been in the habit of handling her hair, and her general health has been good.

Family History.—The mother has a similar but less marked defect in the occipital region. The patient's brother and other members of the family have normal hair.

Examination.—The hair is fair, thin, ragged and dry with small glistening nodes along the hair shafts. There does not appear to be any other ectodermal defect.

Investigations.

(*a*) Microscopic examination : The hair shafts show irregular nodes and brush-like ends. The earliest changes are localized rings where the keratin of the cuticle is altered. The next stage shows nodal swelling with splintering of the cortex resembling a green-stick fracture. Finally the break occurs with brush-like ends. These changes are less marked in the mother's hair.

(*b*) Biopsy of scalp : The number of hair follicles is diminished, and the sebaceous glands are very scarce and small. No intradermal factures of the hair shafts are seen, and the sites of hair keratinization show no abnormality.

Treatment.—Spraying the hair with fine oil and advice on brushing and shampooing has not helped.

Comment.

Trichorrhexis nodosa is a weakness of the hair shaft that results in nodal green-stick fractures occurring at irregular intervals. It should not be confused with moniliform beading of the hair, woolly hair or congenital twisting of the hair, which are quite different congenital abnormalities.

Unlike this congenital example, the acquired type is not uncommon and is usually due to chemical or physical damage such as bleaching or waving of the hair. Another type of this acquired abnormality due to trauma is that seen in the scalp over an infant's occiput due to rubbing the hair on the pillow, or the hairs of a badger shaving brush after long use.

In this child the hair is dry, blonde and brittle and has fractured spontaneously : it has not been broken by handling or the pulling force of brushing. By experiment I found the tensile strength of the hairs to be greater than those of a normal control. The average force required to break a loop of the patient's hair was 76 g., whereas it was 68 g. for those of a control blonde child of similar age.

The patient's hairs could not however withstand lateral forces causing the shaft to bend. By increasing such forces the stages of damage could be ascertained. First, an annular constriction appears and with greater force a disruption of the cuticle occurs until finally the cortex breaks up and the shaft is only linked by the brush-like ends. This could not be reproduced on the normal control hairs.

Histological examination of the scalp shows no evidence of intradermal fractures, nor any abnormal keratinization of the inner root sheath. There was a paucity of hair follicles and the sebaceous glands were immature. If this latter finding has any aetiological significance perhaps the condition will improve at puberty.

An exhaustive study of the literature has not revealed records of any other authentic cases of spontaneous, congenital and inherited trichorrhexis nodosa.

Discussion.

Dr. J. S. Pegum : I should like to make two contradictory suggestions about this. First perhaps the condition is produced by excessive shampooing. The mother told me she shampooed the hair every day and shampoos are supposed to damage keratin. Secondly, perhaps shampooing with Selsun might make the condition better ; since Selsun is said to build bridges between adjacent keratin molecules.

Dr. Martin-Scott : The mother said to-day she had washed it last night, but I understand she only washes it every week or fortnight.

The following cases have been published in *Proc. R. Soc. Med.*, **49**, 1063

Behcet's Syndrome and Thrombosis of Superior Vena Cava.—Dr. R. MacKeith and Dr. Louis Forman.

Discoid Lupus Erythematosus and Cryoglobulinaemia.—Dr. S. C. Gold.

Alopecia with Hyperkeratosis and Follicular Plugging of Scalp due to Hypothyroidism.—Dr. Louis Forman.

Pulmonary and Cutaneous Sarcoidosis.—Dr. D. Sharvill.

The following cases also were shown :

Lupus Erythematosus Profundus with Cirrhosis of the Liver.—Dr. H. C. Meredith.

Bleaching of the Hair due to Chloroquin.—Dr. G. B. Mitchell-Heggs and Dr. R. G. Howell.

Onychauxis, Keratosis Pilaris and Steatomatosis.—Dr. P. R. Montgomery (for Dr. E. J. Moynahan).

Lichen Planus and Unusual Scarring.—Dr. C. M. Ridley (for Dr. J. S. Pegum).

Bullous Dermatitis of the Leg.—Dr. Louis Forman.

BOOK REVIEWS

Clinical Selections in Dermatology and Mycology.*

There are 36 contributors from the Americas to this book, of which 20 are working in South America and Cuba. It was therefore with interest that the book was received, for the approach and views of the dermatologists of Latin America are not generally available to physicians in this country. The solitary contribution from Europe is a short article by Gustav Riehl of Vienna on Tuberculosis of the Skin. The numerous articles devoted to fungus and yeast infections are an indication of the importance of these infections, cutaneous and systemic, in the tropical zones of Mexico through Brazil to the Argentine.

The book is dedicted to the memory of William F. Peterson. The dedication, in poetic turgidity, is to the teacher of the editor who advances Peterson's views that vasospasm is " one of the precipitating factors in the costellation environment responsible for the production of disease ". The first two chapters discuss this conception in relation to diseases of the eye and skin. Vasospasm, one can agree, may be an important factor in diseases associated with weather change. However, it is difficult not to recoil from the statement that central nervous disease including infantile paralysis and multiple sclerosis have a vasospastic pathogenesis. Are we not promised protection from poliomyelitis by virus vaccine therapy and can this virus infection be only a secondary factor to vasospasm in the central nervous system?

Vascular spasm and subsequent injury may localize noxious agents but vascular damage, necrosis and haemorrhage are recognized as an integral part of the picture of specific inflammatory processes. There are other statements which caused confusion in the mind of the reviewer : thus, " the characteristic skin lesions of herpes zoster ophthalmicus are probably due to release in the skin of histamine by antidromic nerve impulses ". One author is quoted who has developed a thesis that ischaemia is a cause of cancer. These statements are indeed thought-provoking, and similar but minor surprises are to be met with throughout the book. The continuous bath for exfoliative dermatitis and dermatitis herpetiformis would not meet approval in this country. The sections on mycotic diseases and leprosy are clear, well set out and informative, but by no means exhaustive.

Cormia's article on the psychosomatic dermatoses and pruritus is a valuable and easily-read summary of the subject. L. F.

Sutton.†

The publication of a new edition of " Sutton " is dermatological event and this new edition is a worthy successor to the noble line of progeny which first appeared in 1916. It is 13 years since the appearance of the amended 10th edition and during this time there have been great and far-reaching changes in medicine—changes which have profoundly affected dermatological thought and therapy. Difficult though it must have been for the author to decide which of many new ideas were going to stand the test of time and warrant inclusion in his book, he has fulfilled this task with distinction.

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* *Clinical Selections in Dermatology and Mycology.* Edited by Frederick Rehm Schmidtt. Springfield, Illinois : Charles C. Thomas. Oxford : Blackwell Scientific Publications. Pp. 505. Price 80*s*. 0*d*.

† *Diseases of the Skin.* R. L. Sutton, Jnr. (1956) 11th Edition. London : Henry Kimpton. Pp. 1479. Illus. 1972. Price £11. 0*s*.

The book, unlike some of the previous editions, is in one volume and some may cavil at its weight but any disadvantages on this count are, in my opinion, outweighed by the advantages of having the whole book in one piece and not having one half separated from the index as in the two-volume editions.

It is obvious that a great deal of thought has been given to saving of space ; the less important matter appears in small but easily legible print and the author has devised a useful condensation of the names of journals given as references. By putting these immedately after the author quoted in the text, he has avoided the duplication of authors' names which is necessary when references are given at the end of a section. These references are very full and although the preparation of a book of this nature must have been a great undertaking, some of them are to articles which were published only a few months before the book was on sale.

A happy feature of this book, as with the other Suttons, is the cogent discussion lucidly presented, the various lines of treatment enumerated—and then the author states categorically what he himself does. It is obvious that this book is written by one who has had a vast experience of handling patients and it is these personal preferences, particularly in therapy, which enhance the value of this book.

The introductory chapters on anatomy, embryology and physiology of the skin are fascinating reading and cover well the modern concepts. Various diseases of the skin are dealt with as far as possible in an aetiological classification, but inevitably the section on " dermatoses of undetermined cause " is next to the biggest in the book. It is exceeded only by " malformations and neoplasms of the skin and adjoining mucosae ".

In reviewing any book, one inevitably looks for mistakes either of fact, opinion or balance but in this book, in spite of careful search, I have been unable to find anything with which I violently disagree. A book written by an author who is prepared to state quite boldly " When I say a patient has parapsoriasis, I mean that he has a rash reminiscent of psoriasis and that I do not know what is the matter with him " is obviously of great worth, written by an honest practising dermatologist and a gold-mine of sound knowledge. The views on cortisone therapy are up to date ; such things as kerato-acanthomata, chloroquine in the treatment of discoid lupus erythematosus, the histological differences of the blistering eruptions, subjects which we in Europe thought we were a jump ahead of our American colleagues, are discussed fully and carefully.

Finally, the illustrations, 1972 of them, are excellent. They are situated near to the relevant text and all have the clarity of the good black and white picture. The index is full and accurate and the binding is good.

I have thoroughly enjoyed reviewing this book ; it is outstanding in its range and by its fund of references is invaluable—in spite of its price, a book for every practising dermatologist and every serious student of the art.

H. R. V.

Isotopes.*

Several excellent accounts of the medical uses of radio-active isotopes are already obtainable. A new publication covering old ground needs particular qualities if its production is to be justified, and this book possesses many excellent points. It is intended to be a simple but comprehensive account of the medical use of isotopes that can be understood by the reader with very little knowledge of the subject, and the dust cover states " this book emphasises a thoroughly practical approach to therapy ". The volume is elegantly produced and although a few relatively incompre-

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* *Therapeutic Use of Artificial Radioisotopes.* Edited by Paul F. Hahn (1956) London : Chapman & Hall Ltd. Pp. 408. Price 80*s*.

hensible physical formulae are encountered in the introductory chapters, it is surprisingly easy to read and absorb, and many readers will consider it a welcome addition to their medical libraries.

Unfortunately, isotope therapy is often more complicated or much less successful than this book leads the reader to believe. Each chapter has been written by recognized experts in a particular field, and the enthusiasm of the pioneer worker is notoriously difficult to control. There is often no attempt made to evaluate the present place of radio-active isotopes in the control of the disease in question, for some chapters make no worthwhile mention of alternative treatment methods and a few statements are frankly inaccurate. In the chapter on the treatment of carcinoma of the cervix by parametrial injections of colloidal gold, it is stated " There is unanimous agreement that irradiation of the lateral pelvis by intra-uterine and vaginal applications of radium, and supplementary external roentgen therapy is usually insufficient to arrest carcinomatous growths completely ". A glance at the Annual Stockholm Report will show that a considerable number of Stage III tumours are radio-curable by conventional methods, and with the advent of supervoltage and telecobalt therapy adequate external irradiation of the pelvic walls becomes a simple matter. That the parametrial injection of gold has not become generally accepted can be clearly seen from the reference list at the end of the chapter. Five of the six references are to publications by the same author.

Professor Hahn has collected together an eminent list of contributors, and some chapters are excellent. The four contributions by British workers fall into this category, but this must be attributable partly to the fact that they all describe uses which have become generally accepted, and which are now routine procedures in many centres throughout the world. On the whole the book is well balanced, and repetition by different authors is largely avoided, although there does not seem to be any need for two chapters on the use of radio-active colloids for the treatment of malignant effusions.

In short, this is a useful book provided the reader recognises its limitations. It is particularly suitable for the intelligent beginner who intends to read more about the subject, but it could be misleading to the novice without critical faculties.

A. M. J.

Periodic Publications of the Medical Encyclopaedia.*

Vol. 31 contains major articles on Nicolas-Favre disease and soft sore, and separate sections on erythematous, urticarial and papular lesions. These naturally cover a very wide field and contain many rare eponymous entities. The account of treatment is more comprehensive than critical and there are numerous references to modern literature. Several shorter articles include interesting accounts of hyperglobulinaemia, purpura, and aphthosis. Among points noted by the reviewer were the absence of any mention of psychological factors in rosacea, and of cholinergic urticaria. Treatment of angiomata is discussed but nowhere is there a suggestion that they should be left alone.

Vol. 33–34 presents an extensive clinical survey of syphilis and of its various serodiagnostic tests and modern treatments. There is also a general account of cancer of all kinds including its incidence in age, race and country, heredity, industrial aspects and finally theories of pathogenesis. This is supported by an extensive bibliography.

F. F. H.

**Recueil Périodique de l'Encyclopédie Médico-Chirurgicale.* 27e Année—1956—Recueil N^e^. 44 et 47–48. Nos. 31 et 33–34.

A German Textbook.*

This is the seventh edition of Schoenfeld's popular *Textbook of Dermatology and Venereology*, written for undergraduates, postgraduates and specialists.

The arrangement of the text remains the same. It has been amplified on dermatology and reduced on venereology, with 98 new pictures. The book is based on the author's 25-years' experience as a lecturer in skin and venereal diseases and evidences his thorough clinical knowledge of both subjects. Considering that the book is also meant for specialists in dermatology it contains rather scanty reference to histopathology of the skin. Pemphigus seems to be an unimportant disease in Germany now ; the chapter on it has not been very thoroughly dealt with, and little emphasis is placed on recent advances in diagnosis. The histology of pemphigus foliaceus shows " oedema, epithelial necrosis, acanthosis and condensation of tissue ". Fogo salvagem is, according to the author, an infectious disease. Pemphigus vulgaris shows an intra-epidermal bulla containing " acanthotic cells ".

The chapter on treatment covers every aspect of traditional and modern methods, but topical sulphanilamide is not entirely condemned, and only moderation in its use recommended. Vitamin and hormone treatment is discussed and much space is given to grenz rays, x-rays, radium, mesothorium, thorium-X and isotopes.

The chapter on venereology deals extensively with the diagnosis and treatment of syphilis. The clinical illustrations are first rate. The clinical manifestations, pathology and treatment of male and female gonorrhoea are thoroughly discussed. There follows a chapter on non-specific urethritis, soft sore, lymphogranuloma inguinale and granuloma venereum. A chapter on prevention of V.D. and a short discussion on sterility completes the book very nicely. H. H.

Aids.†

The demand for this little book is apparent from the emergence of a new edition within three years. It is satisfactory that those who use what may not unfairly be classed as a " cram book " can trust it as an adequate and up-to-date summary. Emphasis on common diseases might be better achieved by enlarging the chapter on eczema which occupies only 20 pages. The authors should feel less hesitation in reinserting a chapter on the skin manifestations of venereal disease since they devote equal space to cutaneous leishmaniasis and leprosy. Even so, they manage their difficult task in fewer pages than authors in the same series devote to clinical pathology or sanitary science and law. P. J. H.

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* *Lehrbuch der Haut- und Geschlechtskrankheiten*. W. Schoenfeld (1956) 7th Edition. Pp. 513. 315 Illus. Stuttgart : Georg Thieme Verlag. Price DM. 44.

† *Aids to Dermatology*, Fifth Edition. R.M.B. MacKenna and E. Lipman Cohen (1957). London : Ballière, Tindall & Cox. Pp. 312. Price 10*s*. 6*d*.

CORRESPONDENCE

The Editor, 'The British Journal of Dermatology'.

SIR,—I have read with interest the letter from Dr. F. F. Hellier (**68**, 342) and the comment on it by Dr. F. Ray Bettley (**69**, 33). These communications rather neatly summarize two somewhat opposing views as to the best system of dermatologic training. The department of which I am the director had the very considerable pleasure of Dr. Hellier's company for a few days. During his visits to dermatologic training centers it was possibly more expedient, within a short period, for us to demonstrate some of the American "genius" for over-organization, than to outline the philosophy behind the training programs in an increasing number of American centers. In any event, I would disagree that there is an increasing trend toward didactic methods in the U.S.A. in the training of young physicians to be specialists in dermatology.

Following World War II, there was a great flood of applications for training in all specialties of medicine and surgery, from physicians whose careers had long been interrupted by the War. In attempting to meet this demand, several training centers organized informal or formal didactic courses. Because the basic science personnel available to most departments of dermatology was very limited, lecturers for such courses were recruited from pre-clinical departments, whether or not the lecturers had any interest whatever in the skin. On the whole these "visiting professors" did an excellent job, but I suspect that most of them were considerably relieved when the press of applicants for training in dermatology subsided. One by one these courses folded their tents, and there now remain only two long-established centers which regularly offer one year of formal didactic training in the basic sciences and in clinical dermatology. These courses perform an excellent service for certain types of students, and are receiving an increasing number of applications from graduates of foreign medical schools.

I would agree that excellent dermatologists often are developed from the student-teacher association of a well-trained young physician, with experience in several fields of basic science, and an experienced clinician with true competence in laboratory work of various types. There are few of the former, and almost none of the latter, and hence some compromises are necessary. Dermatology is a rapidly broadening specialty in the U.S.A. The training of the complete dermatologist is no easy matter, and I would venture to state that there are no more than six or seven centers in the United States where the facilities are adequate to do this properly. In judging the effectiveness of dermatologic training centers, one must not fall into the trap of using performance in Specialty Board examinations as a chief criterion. Those physicians who will become great teachers, outstanding investigators, or superb clinicians are not necessarily the same as the individuals who, by a variety of methods, store away thousands of more or less unrelated facts, to be spewed forth at the proper moment without, necessarily, any reasoned correlation of these facts. All Specialty Board bodies in America have long been concerned about the stimulus which their examinations may give to the development of individuals of this type. As a result, each Board has scrutinized its examinations continuously in an effort to have them indicate those individuals who can *think* rather than those who just *know*. I recall clearly a remark by the late J. Gardner Hopkins in his presidential address to the American Dermatological Association, to the effect that it worried him when his trainees did too well in their specialty qualifying examinations, because it indicated they they had spent too much time in the study of things less worthwhile.

To my own way of thinking, the only justification for all-inclusive didactic courses in relation to dermatology is in those fields in which there is no adequate text available.

The list of such fields is becoming smaller. Twenty-five years ago, such special monographs and texts were almost non-existent, but now the fields of dermatologic pathology, mycology, chemistry, physiology, radiophysics, virology and bacteriology are more adequately covered. From this point on, conferences and seminars are justified chiefly insofar as there is an individual in the department concerned whose knowledge is in advance of what can be found in the monographs and texts. It is also useful to give demonstrations of the applications of these sciences to clinical practice, and to afford the student some experience in the laboratory. Dermatopathology seminars, on the basis of slide collections and the current biopsies in a department, are worthwhile. Group presentations of selected individual patients by a master clinician are certainly valuable. No one can doubt that, for the physician whose chief ultimate goal is the diagnosis and treatment of disease in man, the privilege of working day after day under the close supervision of a competent preceptor is the most valuable and essential experience of all, but the trainee must be regarded as a true associate, not as a cheap assistant to " make tea ". Because of occasional abuses, the preceptor type of training has been increasingly restricted and regulated in the U.S.A.

I am in particular agreement with Bettley's feeling that graduate training in medicine should not follow a rigid schedule. On the other hand, such training cannot be completely haphazard, and some orderliness is necessary. After an initial exposure of six months or so to the various disciplines within the specialty, it appeals to me as positively wicked to encase the trainee in a schedule so rigid that he cannot to some extent suit his own particular needs and interests. The rudiments of clinical dermatology are not too difficult to absorb, and if the candidate needs several years of set courses and clinics to accomplish this, he probably should not be in medicine at all, to say nothing of aspiring to particular expertness in a special branch of medicine. Some trainees aspire only to a superior brand of clinical service, and this is a high calling. Others, occasionally, " catch fire " in regard to investigative work, and this constitutes a most rewarding experience for any chief of a service, because it is these enthusiasts who will ultimately contribute to real advances in dermatologic knowledge, and will attract favourable notice from science and medicine in general. They will also, I submit, be better clinicians as a rule, because of their investigative experience.

One final thought. Achievement of the ideal system of specialty training is not through rules set down by committees or regulatory bodies of any sort, though such bodies furnish a useful means of exchange of ideas and discussion of common problems. The final actions of almost all committees represent a series of compromises ; not infrequently the best official position which can be achieved is some five or ten years behind the times. If such a body ventures much further than this, it will be regarded in bureaucratic circles as too *avant garde* to be trustworthy. Real advances are made through the efforts of those centers in which there is a determination to proceed in the true tradition of a university, not a trade school. There must also, I think, be some centers which are intelligently venturesome, with a " damn the torpedoes, full speed ahead " attitude which may occasionally result in one's ship brushing a few rocks, but from which one has the not inconsiderable pleasure of welcoming aboard an increasing number of new shipmates of ever higher competence and stature.

Sincerely yours,

DONALD M. PILLSBURY.

Department of Dermatology,
University Hospital,
University of Pennsylvania, U.S.A.,
March, 1957.

CURRENT LITERATURE.

IDIOPATHIC HYPERLIPAEMIC AND PRIMARY HYPERCHOLESTERINAEMIC XANTHOMATOSIS. VII : EFFECTS OF INTRAVENOUSLY ADMINISTERED FAT ON THE SERUM LIPIDS. W. F. Lever and W. R. Waddell. (1955) *J. invest. Derm.*, **25**, 233.

In 13 of the 14 control subjects and in all 4 patients with P.H.X. the serum fat had returned to normal within 4 hours. In the 6 most severe of the 9 cases of idiopathic lipaemia it remained elevated for at least 8 hours. Any raised blood cholesterol levels that had previously existed in the subjects of this experiment were found later to have been substantially reduced and in 3 of the patients with idiopathic lipaemia there appeared to have been some improvement in their capacity to eliminate lipids from the blood stream. J. H. T. D.

THE EFFECT OF NON-MEDICAMENTOUS ENCLOSURE AND " DERMATOLOGIC REST " ON ECZEMA. R. D. G. Ph. Simons. (1955) *J. invest. Derm.*, **25**, 365.

One hundred patients with chronic eczema were treated with occlusive dressings of plaster of paris, with or without immobilization, in an attempt to answer the questions : does the hospital in-patient recover because of psychological physical or cutaneous rest, or because he is protected from allergens ; or, if by means of ointments, etc. (in which the author *hastens to add* that he firmly believes), why do so many different formulae have much the same effect ? The author makes it clear that he does not recommend the method of surgical or cutaneous rest as a routine treatment for eczema but that he is trying to isolate one of the factors supposed to contribute to the benefits of hospitalization in the hope of demonstrating physical rather than emotional causes for what he calls " sanatio spontanea nosocomialis ".

Any attempt to introduce science into a realm where superstition at present reigns unchallenged should be treated with respectful sympathy ; and we may well reflect that it is probably beyond human ingenuity to devise a fruitful experiment in which all the relevent quantities are unknown. The factor he has attempted to isolate—occlusion—is in itself unbelievably complex and it is not clear that the author has taken stock of all the familar phenomena : for example the extinction of many eruptions by the pressure of shoulder straps, garters and ankle boots or the opposite tendency for the eczema that is provoked by an injury to spread under the plaster of paris splint and often to occupy exactly the area covered by it, to mention only two of them.

His interpretation of results would not be universally acceptable. For instance he believes that infantile facial eczema is not cured by occlusion because the infant can enjoy all the advantages of scratching by pulling faces inside the plaster ; and he uses the hypothesis contained in the impressive term " Mitreaktion " to explain why untreated areas sometimes do equally well during a therapeutic procedure having obsession-assuaging entertainment value. But if the purpose of the paper was to stimulate thought and to provoke new ideas it should succeed.

J. H. T. D.

THE INTERMEDIARY CARBOHYDRATE METABOLISM OF EPIDERMIS. II ASSAY FOR SUCCINIC DEHYDROGENASE AND CYTOCHROME OXIDASE. R. D. Griesemer and E. Gould. (1955) *J. invest. Derm.*, **25**, 383.

It has been thought possible that changes in enzyme activity might help to betray or even to explain certain disorders of function or structure—as, for example, in carcinoma. The authors describe their assay of these enzymes in rat epidermis. The method employs the Warburg manometer and since the two enzyme systems are interdependent the answer given in terms of total oxygen uptake has to be differentiated by varying the conditions and concentrations of reagents used. J. H. T. D.

ISOLATION OF THE NUCLEOTIDES OF RIBONUCLEIC ACID FROM THE SKIN OF YOUNG RATS. I. A. Bernstein and W. P. Block. (1955) *J. invest. Derm.*, **25**, 375.

The turnover of the various organic compounds within a tissue can be estimated from the rate at which they incorporate an isotope tracer.

This work is concerned with the separation of nucleic acid compounds and their identification, in preparation for an assay of their radioactivity.

The nucleotides are adsorbed from the crude extract by an ion-exchange resin, washed out again with ammonium formate, separated by a process analogous to chromatography and finally identified by their absorption bands in the U.V.L. spectrum. J. H. T. D.

STUDIES ON TYROSINASE REACTION. II: STUDIES ON THE NEW METHOD OF TYROSINASE REACTION. Y. Yoshida and Y. Togashi. (1955) *J. invest. Derm.*, 25, 363.

Meaning has presumably been lost in the process of translation. For example "approximately 3 × 3 mm. slices . . . " No doubt the third dimension may be disregarded in the case of extremely thin slices; but later we are asked to imagine that " . . . slices were injected intracutaneously . . . " J. H. T. D.

THE WATER CONTENT OF THE STRATUM CORNEUM. III: EFFECT OF PREVIOUS CONTACT WITH AQUEOUS SOLUTIONS OF SOAP AND DETERGENTS. I. H. Blank and E. B. Shappirio. (1955) *J. invest. Derm.*, 25, 391.

Slices of callosity from the human foot weighed after desiccation and weighed again in atmospheres of known relative humidity were then treated by immersion for 3 hours at 40° C. in water and in various solutions of soap builders and detergents; retested for their hydrophilic capacity, and the solutions assayed for nitrogenous material extracted. The answer failed to support the view that detergents are more harmful to the horny layer than pure soap. The interesting fact emerged during discussion that only by swabbing the skin with a CO_2 snow acetone mixture can "chapping" of the skin be brought about in the summer months. J. H. T. D.

FACTORS INFLUENCING THE INCIDENCE OF EPIDERMAL METHYLCHOLANTHRENE TUMOURS IN MICE TREATED WITH CORTISONE. F. Herrmann, R. W. Sherwin, S. D. Morrill, M. J. Rothstein and M. B. Sulzberger. (1955).

I: EXTERNAL APPLICATION OF METHYLCHOLANTHRENE COMBINED WITH CORTISONE ADMINISTRATION AND BIOPSY TRAUMA. *J. invest.Derm.*, 25, 403.

II: INFLUENCE OF VARIATIONS IN THE TIMING OF CORTISONE ADMINISTRATION IN RELATION TO CARCINOGEN APPLICATION. *J. invest. Derm.*, 25, 411.

III: STUDIES OF THE HAIR FOLLICULAR CYCLE IN RELATION TO THE INCIDENCE OF TUMOURS AFTER CORTISONE ADMINISTRATION. *J. invest. Derm.*, 25, 423.

The reaction of mouse skin to this carcinogen is stronger during the follicular resting phase and that is prolonged by cortisone: thus neoplastic change is accelerated.

Whether treatment with cortisone continued indefinitely after application of the carcinogen might inhibit tumour formation is another matter, not dealt with in this important series of experiments. J. H. T. D.

THE HISTOLOGY OF THE HUMAN EAR CANAL WITH SPECIAL REFERENCE TO THE CERUMINOUS GLAND. E. T. Perry and W. B. Shelley. (1955) *J. invest. Derm.*, 25, 439.

Those interested in the anatomy of the skin who haven't time to read this succinct and delightful account must at least glance at the photomicrographs. The reviewer's only criticism is concerned with the authors' teleological concept of the cerumen acting as "nature's fly-paper". Indeed he can imagine nothing more distracting than to have a small but energetic fly on the wall of his auditory meatus. J. H. T. D.

LOCAL APPLICATION OF 8-METHOXYPSORALEN IN VITILIGO. E. W. Kelly and H. Pinkus. (1955) *J. invest. Derm.*, 25, 453.

Of 20 patients only one was subjected to simultaneous paired comparison, and that with equivocal result. The remedy is applicable only to small areas of short duration and the results are better in Neroes (sic). J. H. T. D.

HEREDITARY PELLAGRA-LIKE SKIN RASH WITH TEMPORARY CEREBELLAR ATAXIA, CONSTANT RENAL AMINO-ACIDURIA AND OTHER BIZARRE BIOCHEMICAL FEATURES D. N. Baron, C. E. Dent, H. Harris, E. W. Hart and J. B. Jepson. (1956) *Lancet*, ii, 421.

The authors describe a new disease which they call H disease after the name of the affected family. Four of eight children of a first cousin marriage were affected with an eruption on the

uncovered areas that occurred after exposure to sunlight. In two children this appeared identical with the skin changes of pellagra. Severe but fully reversible cerebellar ataxia developed in association with the rash. The older children are mentally retarded. All the affected children showed a gross amino-aciduria of constant pattern as well as a large excretion of indole-3-acetic acid and less constantly indican. The authors suggest that the primary disorder in this condition is a metabolic block on the pathway from tryptophane to nicotinic acid. They also suppose that some enzyme systems requiring nicotinic acid can only obtain their supply from the metabolism of tryptophane and not from dietary nicotinic acid. This would explain the close similarity of some of the clinical features to those of true pellagra as well as the occurrence of various indole metabolites in the urine R. H. M.

CAT-SCRATCH FEVER. R. L. Lyon. (1956) *Lancet*, ii, 555.

A case of cat-scratch fever is described which showed recrudescence of lymphadenitis and skin eruption (described as morbilliform as well as on occasion resembling erythema multiforme and erythema marginatum) after injection of cat-scratch antigen. This injection produced no local effect. R. H. M.

ADVANCES IN THE TREATMENT OF SKIN DISEASES. J. G. Downing. (1956) *Practitioner*, **177**, 403.

For the control of cutaneous infection careful selection of an antibiotic is necessary. Penicillin is still the most efficient, the least toxic and the least expensive. Streptomycin is useful in cutaneous tuberculosis, but should never be used topically. Chloramphenicol is a dangerous drug and should be used with great care. Tetracycline in oral doses of 1 to 3 g. daily is useful in acute pyogenic infections. Erythromycin has occasional value in impetigo or sycosis vulgaris. Neomycin has a low index of sensitization and is chiefly used as a compress or an ointment.

Corticotropin and cortisone have great value in the treatment of systemic lupus erythematosus and pemphigus, and when combined with local therapy shorten the course and reduce the discomfort in acute inflammatory generalised eruptions, such as urticaria, dermatitis venenata, drug eruptions and erythema multiforme. A few days of treatment should be sufficient in such acute cases. This method of treatment has little value, apart from temporary relief, in chronic, non-fatal or recurrent dermatoses.

Mepacrine and chloroquine benefit light-sensitive dermatoses and tannic acid and para-amino-benzoic acid are useful as protective sun-screens. Nystatin used orally or locally is effective against monilia, and in actinomycosis a combination of penicillin, sulphadiazine and X-ray therapy is effective.

Other therapeutic agents discussed include isoniazid for cutaneous tuberculosis, " Diasone " for dermatitis herpetiformis, antihistamines, selenium sulphide emulsion as a shampoo and " Prantal " as an ointment for some cases of persistent vesiculation of the palms. R. J. C.

THE SKIN AND PSYCHOSOMATIC DISEASE. E. C. Ritter. (1956) *Practitioner*, **177**, 598.

Psychological factors are important in the following conditions : eczema, rosacea, lichen planus, alopecia areata, vitiligo, psoriasis, acne vulgaris, pruritus, hyperidrosis and allergic reactions. Treatment should be directed to reducing the patient's mental stress. In certain cases the help of a psychiatrist, an almoner or a priest may be enlisted. R. J. C.

PIGMENTED SKIN LESIONS. B. K. Rank. (1956) *Practitioner*, **177**, 605.

Pigmented lesions include junctional, intradermal and compound naevi. Activated junctional naevi may be pre-malignant, as may compound naevi, by virtue of their junctional activity. A diffuse junctional naevus first appears in adult life, often occurring on the face of post-menopausal women, and is pre-malignant. Small junctional naevi on the hands, feet and genitalia may also be precursors of malignancy and should be removed. Malignant melanomata may be superficial or spread deeply into the dermis; they are treated by block excision and possibly gland field dissection. It is important to distinguish these lesions from angiomata and pigmented basal-cell epitheliomata. R. J. C.

SKIN HISTAMINE : ITS LOCATION IN THE TISSUE MAST CELLS. James F. Riley and G. B. West. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 471.

The authors detail experiments made to determine the mast cell and histamine content of various layers of the skin in some half-dozen of the lower animals and in man. Amount of histamine

present always varied in proportion to the number of mast cells seen. This helped to lead to the conclusion that the bulk of extractable histamine in skin is located in the tissue mast cells.

J. K.

DIABETES AND PSORIASIS. Smith H. Gibson and Harold O. Perry. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 487.

From a study of 29 patients with psoriasis and a control series of 27 patients the authors conclude that there is no reason to presume that diabetes and psoriasis are related. J. K.

CUTANEOUS CHANGES DURING THE MENSTRUAL CYCLE. Frederick Kalz and Allene Scott. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 493.

This article details the observations made in 60 patients; 50 of them suffered from pre-menstrual tension and exacerbation of their dermatoses and 10 (5 males and 5 females) were controls. Fluid retention appears to play a significant role in pre-menstrual exacerbations of acne vulgaris and other dermatoses as well as in the pre-menstrual tension syndrome. Tablets containing ammonium chloride (as well as 7 other ingredients) given for ten days before the onset of menstruation effectively controlled both manifestations. J. K.

ECCRINE POROMA. Hermann Pinkus, James R. Rogin and Perry Goldman. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 511.

The authors describe 5 examples of a small benign neoplasm occurring on the non-hairy surface of the foot resembling papilloma or granuloma pyogenicum. Histologically they were tumours of the epidermal sweat duct unit and the name given in the title is suggested for this group of the benign solid hidradenomata. J. K.

THE USE OF DETERGENT-VITAL STAINING IN DIRECT MICROSCOPIC EXAMINATION OF SCALES ETC. PRELIMINARY CONCLUSION. A. Delmotte, G. Achten and K. T. Wang. (1956) *Arch. belg. Derm. Syph.*, **12**, 81.

ANTIFUNGAL ACTION OF DETERGENTS. G. Achten. (1956) *Arch. belg. Derm. Syph.*, **12**, 91.

The first article, after dealing with detergents in general, describes the difficulty of finding a detergent that will clear the scales and at the same time allow staining. Cationic detergents cause scales of inflammatory origin to disintegrate. The advantages and limitations of this method are discussed.

The second paper deals with the action *in vitro* of various detergents on the growth of dermatophytes. Some are successful inhibitors, some unsuccessful and some show a moderate effect on growth. The formulae of the detergents used are given, which is useful as their names are quite strange. J. K.

GLYCOGEN IN THE HUMAN SKIN. G. Achten. (1956) *Arch. belg. Derm. Syph.*, **12**, 100.

Glycogen is never found in the basal layer of the epidermis and lower part of the malpighian layer, nor is it found in the granular and the horny layers. It is found in variable amount in the middle of the malpighian layer. It may be assumed that glycogen is used as a source of energy in the active lower layers of the epidermis; the middle part of the malpighian layer is comparatively inactive and thus stores glycogen but it disappears in the superficial layers where it is used as a source of energy in the production of keratin. J. K.

MERCURY ABSORPTION AND PSORIASIS. P. M. Inman, R. Gordon and P. Trinder. (1956) *Brit. med. J.*, ii, 1202.

Patients with psoriasis, treated with ointment containing mercury either as ammoniated mercury (approx. 2%) or yellow oxide (10%) applied twice daily with occlusive dressings, were investigated by examining their urine for evidence of absorption of mercury. The ointment base was either soft paraffin or equal parts of soft paraffin and lard. The areas of skin treated (more extensive than the psoriasis) varied, most being 25 to 90% of the total body surface. The majority of the 24 patients were women and children. Of these 22 had a concentration of mercury in the urine higher than the normal. Nevertheless, there was no clinical evidence of toxicity.

S. T. A.

FUNGOUS DISEASES OF BRITAIN. R. W. Riddell. (1956) *Brit. med. J.*, ii, 783.

This is a useful review of the present position. Superficial and subcutaneous mycoses as well as systemic infections are considered. S. T. A.

HISTOPLASMOSIS CONTRACTED IN BRITAIN. W. St. C. Symmers. (1956) *Brit. med. J.*, ii, 786.

The first report of infection with histoplasmosis acquired in this country. The patient, a man, cut his forehead on a flint path and developed a condition like sarcoidosis which ran a benign course over three years. Fourteen years later a siliceous granuloma appeared in the scar and after six months there was generalized lymphadenopathy which settled during the following year. After three more years, however, lymph nodes again became enlarged and from them *H. capsulatum* was isolated by culture. S. T. A.

PANANGIITIS HAEMORRHAGICA LIPOIDICA. G. Stuttgen. (1956) *Derm. Wschr.*, **134**, 1149.

Under this name the author describes a purpuric eruption of both upper and lower extremities but more marked in the latter in a woman aged 62 who had hypertension, hypercholesterolaemia and lipaemia. Histologically the lesions showed perivascular infiltration with histiocytes and leukocytes. He considers the condition to be inflammatory in origin with secondary impregnation of the perivascular areas with Sudan III-positive substances as the result of the high blood lipoid level. Hydrocortisone therapy caused fading of existing and prevention of new lesions.

W. G. T.

THE TREATMENT OF VITILIGO WITH MELADININE. H. Teller. (1956) *Derm. Wschr.*, **134**, 1153.

Only 5 cases were treated, two with moderate success. The other three did not improve but the occurrence of photosensitization in one of these appears to justify publication. Shortly after the first irradiation with ultraviolet light. the patient developed much urticarial erythema and this recurred 2 weeks later when the treatment was resumed and irradiation was given for 15 seconds only. Severe photosensitivity required admission to hospital and persisted for $3\frac{1}{2}$ months. Intestinal dysbacteria and indicanuria was found and the former was treated. W. G. T.

LIVEDO RETICULARIS IDIOPATHICA ET SYMPTOMATICA. J. J. Herzberg. (1956) *Derm. Wschr.*, **134**, 1045.

This malady belongs to the group of endangiitic changes of arterioles and consists of recurrent ulceration with occasional necrosis of peripheral sections of limbs. Obstruction or occlusion of arterioles leads to dilatation of the venous part of the capillaries and of venules and produces in this disease partly sharply defined, partly less distinct areas of alteration in the appearance of the skin. It varies from cutis marmorata, which is an angiospastic condition of the skin, to haemorrhagic infarction, ulceration and necrosis ; the majority of cases lie between these extremes. The disease is almost entirely confined to women between the ages of 17 and 54 and is accompanied at times by acrocyanosis, perniosis, hyperidrosis and a lowered tolerance of cold. The livid reticulation is most commonly seen on legs and thighs and on the insteps, more rarely on the upper extremities. The obstruction is caused by intimal proliferation and thickening of the media. Differential diagnosis is from obliterating arteriosclerosis, perniosis, acrocyanosis, ulcerating and necrotizing vasculitis and Raynaud's phenomenon, which can however occur in conjunction with it. It is is never seen in endarteritis obliterans. The aetiology is unknown. Occasional results of sympathectomy suggest a disturbance of nervous control. Good results of treatment of focal sepsis and the use of cortisone and antibiotics are in favour of an additional infective or allergic mechanism. W. G. T.

UNUSUAL LINEAR PALMAR AND PLANTAR KERATOSIS WITH DORSAL HYPERKERATOSES. G. Brehm. (1956) *Derm. Wschr.*, **134**, 1173.

The group of atypical keratoses shows a great number of peculiarities and the question of their inheritance has not yet been settled. In this respect they differ from keratoma palmare and plantare and Mal de Meleda, which are dominant and recessive respectively. The reported case which showed linear striation of the palms, mostly over the thenar and hypothenar eminences and radiated towards the finger, gave no family history of the malformation. There were nodular dorsal hyperkeratoses. The plantar surfaces of the feet were affected in the pressure areas only. In

addition there were accessory nipples and warty naevi of the axillae and groins. The possibility of an embryopathy is considered since the mother had a serious accident during pregnancy but since this happened in the fifth month it probably does not explain the manifestation.

W. G. T.

LEUKONYCHIA AS AN OCCUPATIONAL DISEASE. M. Thal. (1956) *Derm. Wschr.*, **134**, 1178.

Punctate leukonychia is frequently seen, striate leukonychia even more often, but total leukonychia is rare. The punctate variety is considered to be traumatic in origin, whereas the aetiology of the other two forms is not certain and various causes have been stated. Chemical substances such as acids, alkalis and nitrates have been reported as causing these changes. Three cases of leukonychia occurring in patients engaged in the meat preserving industry are reported. The noxious agent was a solution containing nitrites and nitrates. The changes were reversible and the application of acrylic resins protected one of the cases. Histological changes were thought to be due to oedema in these occupational cases, whereas in those of other aetiology they were explained by parakeratosis.

W. G. T.

ALOPECIA TOTALIS AFTER DESACETYLMETHYLCOLCHICINE THERAPY OF GOUT. W. M. Mikkelsen, R. S. Salin and J. F. Duff. (1956) *New Engl. J. Med.*, **255**, 769.

Loss of nearly all the hair on the scalp in a man treated with desacetylmethylcolchicine for gout is described; similar occurrences after the use of this drug are mentioned.

A. D. P.

OBSERVATIONS ON URTICARIA IN CHILDHOOD. J. H. Schwartz. (1956) *New Engl. J. Med.*, **255**, 771.

Of 27 children with urticaria observed for 17 months, only 5 have recurred. This, with the absence of eosinophilia and failure to respond to antihistamines, makes the author think that urticaria in childhood is not generally due to allergy. He suggests that it may be a manifestation of a specific but unknown infectious exanthem.

A. D. P.

A NEW EFFECTIVE SHAMPOO TREATMENT IN SEBORRHOEA CAPITIS. E. F. Finnerty. (1956) *New Engl. J. Med.*, **255**, 614.

A new shampoo is described, containing anionic detergents and wetting agents with sulphur, salicyclic acid and hexachlorophene. The author states that treatment with the shampoo "is at least 95% effective in the control of dandruff, seborrhoea oleosa and seborrhoeic dermatitis". Occasionally excessive dryness of the scalp is produced.

A. D. P.

PAROXYSMAL NOCTURNAL PORPHYRINURIA. HERETOFORE UNDESCRIBED MANIFESTATION OF CHRONIC PORPHYRIA. J. A. Smith and A. M. Freemin. (1956) *New Engl. J. Med.*, **255**, 705.

Large amounts of uroporphyrin and coprophyrin were found to account for "bloody urine" passed by a negro each morning. As the day progressed the urine became lighter in colour, but lying down always caused it to become dark again. The skin of the face, hands and abdomen was abnormally pigmented.

The authors emphasize the effect of posture on the excretion of porphyrins and say this has never been described previously.

A. D. P.

NONTHROMBOCYTOPENIC PURPURA DUE TO MILTOWN. (2-METHYL-2-N-PROPYL-1, 3 PROPANEDIOL DICARBAMATE). W. J. Carmel and T. Danneberg. (1956) *New Engl. J. Med.*, **255**, 770.

Three cases of acute nonthrombocytopenic purpura secondary to Miltown are reported. Reactions occurred after 1–3 tablets were taken for the first time.

A. D. P.

CARCINOMA OF THE LIP. P. M. Burke and F. S. Hopkins. (1956) *New Engl. J. Med.*, **255**, 552.

The records of 182 patients with histologically proved squamous carcinoma of the lip were analysed. Males predominated as usual, and when allowance was made for patients dying from other causes, there was an 80% survival rate without recurrence after five years. The results

of surgical treatment and radiotherapy were approximately equal in comparable lesions. Routine removal of the lymph glands in the neck is not recommended unless they are enlarged.

A. D. P.

NON-BACTERIAL REGIONAL LYMPHADENITIS. (CAT-SCRATCH FEVER). W. T. Small and R. C. Sniffen. (1956) *New Engl. J. Med.*, **255**, 1029.

It is suggested in this paper that when symptoms of cat-scratch fever have lasted for several weeks and the patient is unable to carry on his normal activities, the best treatment is excision of the affected lymph glands. The excellent results of this procedure in 6 patients is described, each of whom was rapidly restored to normal health. A. D. P.

CONTACT DERMATITIS FROM CHLORPROMAZINE HYDROCHLORIDE. R. F. Tilley. (1956) *New Engl. J. Med.*, **255**, 1046.

Dermatitis in 8 persons who handled chlorpromazine began on the hands and spread to arms, neck and face, and a patch test was positive in all after 72 hours. A. D. P.

FAMILIAL OCCURRENCE OF DISSEMINATED LUPUS ERYTHEMATOSUS. S. Glagov and E. Geckman. (1956) *New Engl. J. Med.*, **255**, 936.

Systemic lupus erythematosus occurring in a woman aged 44 and her daughter aged 18 is described in detail and various hypotheses that might explain the familial connection are considered. A. D. P.

ALLERGIC ECZEMATOUS CONTACT DERMATITIS DUE TO METALLIC NICKEL. A. A. Fisher and A. Shapiro. (1956) *J. Amer. med. Ass.*, **161**, 717.

Nickel is now a familiar cause of contact dermatitis but this careful account of 198 cases raises several points of interest. Among the more unusual sites of origin were the lips (bobby pins held in the mouth), the sole of the foot (metal arch-support) and antecubital fossae (handbags). The hands and fingers were frequently affected from contact with articles such as scissors, knitting needles or door-handles. Various methods of covering nickel objects to permit their continued use are described. A 5% solution of nickel sulphate is recommended for patch-testing. Of 40 patients who were re-tested after intervals of 2 to 17 years, 90% retained their sensitivity.

A. J. R.

UNUSUAL SKIN LESIONS ASSOCIATED WITH THROMBOSIS OF SUBCLAVIAN ARTERY. M. H. Samitz and S. Lisker. (1956) *J. Amer. med. Ass.*, **161**, 725.

A man aged 53 developed fissuring and ulceration of the tips of the index and little fingers of the left hand associated with severe pain. The clinical features originally simulated a fungous or bacterial infection, but other findings betrayed the vascular origin of the lesions, which proved to be secondary to thrombosis of the subclavian artery. A. J. R.

PLAQUENIL IN THE TREATMENT OF LUPUS ERYTHEMATOSUS. J. F. Mullins, F. L. Watts and C. J. Wilson. (1956) *J. Amer. med. Ass.*, **161**, 879.

Plaquenil is the hydroxyethylamino analogue of chloroquine diphosphate. It was given in an initial dose of 600–2400 mg. daily to 40 patients with lupus erythematosus. In the chronic discoid, localized oedematous and subacute types it was as effective as chloroquin and was sometimes better tolerated. Nausea or vomiting were the commonest side effects, but were rarely encountered. Maintenance dosage ranged from 400 to 2000 mg. daily. A. J. R.

WAYS AND MEANS TO SAFE SUNBATHING. COMMITTEE ON COSMETICS. (1956) *J. Amer. med. Ass.*, **161**, 1480.

This sensible article considers many practical points often omitted by more technical publications; dermatologists will find here some help in answering the sometimes searching questions of their more fashion-conscious patients. A. J. R.

THROMBOCYTOPENIC PURPURA RESULTING FROM SULFIZOXAZOLE (GANTRISIN) THERAPY. T. W. Green and J. Q. Early. (1956) *J. Amer. med. Ass.*, **161**, 1563.

Gantrisin has been regarded as one of the safest sulphonamides. Two cases in which it gave rise to thrombocytopenic purpura are briefly reported. A. J. R.

FATAL VACCINIA ASSOCIATED WITH CORTISONE THERAPY. S. Olansky, J. G. Smith Jr. and O. C. E. Hansen-Pruss. (1956) *J. Amer. med. Ass.*, **162**, 887.

Fatal generalized vaccinia developed in a woman aged 42 who was receiving cortisone for chronic lymphatic leukaemia. She had been vaccinated for the treatment of herpes simplex of the lip. A. J. R.

GRANULOMA OF THE AXILLA CAUSED BY DEODORANTS. L. Rubin, A. H. Slepyan, L. F. Weber and I. Neuhauser. (1956) *J. Amer. med. Ass.*, **161**, 953.

A new eruption of the axillae, provoked by deodorants and antiperspirants is reported. Four cases are described and 11 others mentioned. The lesions are small dull brownish-red papules, shining and somewhat translucent, developing in large numbers within a few days of the application of the deodorant. In some cases erythema or dermatitis may precede or accompany the eruption, and pruritis is always present. The lesions are persistent and resistant to treatment. Histological examination has consistently shown a tuberculoid granuloma. The cause of the granuloma is uncertain. The deodorant-stick used by 3 patients contained zirconium, but the lotion applied by the fourth patient contained chlorhydroxyaluminium sulphate but no zirconium.

A. J. R.

IDENTIFICATION OF MALIGNANT POTENTIALITIES OF MELANOCYTIC (PIGMENTED) NAEVUS. B. Shaffer. (1956) *J. Amer. med. Ass.*, **161**, 1222.

The author prefers the term melanocytic naevus for the simple pigmented mole. Since only those naevi with junctional activity possess malignant potentialities he has attempted to determine which clinical types are liable to show this histological feature. Flat or slightly elevated naevi, elevated naevi with pigmented haloes, and verruciform lesions frequently show junctional activity, whilst polypoid, dome-shaped, sessile and pedunculated lesions seldom do so. A. J. R.

PHYSICAL AND PHYSIOLOGICAL CLUES FOR DIAGNOSING ECZEMA. W. C. Lobitz Jr. and R. L. Dobson. (1956) *J. Amer. med. Ass.*, **161**, 1226.

This is an admirable summary of the structural and functional characteristics which determine the reactions of the atopic subject. The dryness of the skin, the constant cutaneous vasospasm, and distinctive responses to acetylcholine and to histamine are among the features which distinguish the atopic from the remaining 90% of the population. The clinical management of atopic eczema is greatly assisted if the patient can be given some understanding of the nature of the problems involved. A. J. R.

SQUAMOUS CELL CARCINOMA OF ABDOMINAL WALL. E. L. Strohl and R. E. Land. (1956) *J. Amer. med. Ass.*, **161**, 1473.

The brief report of a squamous-cell carcinoma, measuring 14 × 12 cm. on the abdominal wall of a woman aged 66. Although the inguinal glands were involved the patient was alive without clinical evidence of metastasis or recurrence over a year after radical excision.

A. J. R.

PREDNISONE IN THE MANAGEMENT OF IDIOPATHIC HEREDITARY LYMPHOEDEMA (MILROY'S DISEASE). T. C. Panos. (1956) *J. Amer. med. Ass.*, **161**, 1475.

A girl, aged 11, with idiopathic hereditary lymphoedema involving both lower legs suffered recurrent attacks of fever, pain, redness and swelling. Prednisone produced an 80% reduction in the oedema and no further attacks developed. After a month a maintenance dose of 5 mg. daily was established and has been continued for 14 months. A. J. R.

CUTANEOUS SENSITIVITY REACTIONS TO CHLORPROMAZINE. J. F. Mullins, I. M. Cohen and E. S. Farrington. (1956) *J. Amer. med. Ass.*, **162**, 946.

The study of 85 patients with skin eruptions due to chlorpromazine. The 75 patients who had reacted to the systemic administration of the drug presented a wide variety of eruptions: erythematous or morbilliform 47, photosensitization 18, urticarial 7, purpuric 2, bullous 1. The erythematous eruptions included some of seborrhoeic type. In most cases the dose of chlorpromazine had been about 600 mg. daily. The eruption cleared rapidly when the drug was discontinued or when the dose was decreased. The remaining 10 cases were contact dermatitis. When interpreting patch tests it must be remembered that full-strength chlorpromazine is a primary irritant.

A. J. R.